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Analysis of surface modification effect of polymer membranes on the interaction with blood components and microorganisms

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By now there is developed a number of polymer and composite materials for bioartificial organs, products of medical purpose and membranes with a complex of positive physicochemical and biological properties. But none of the materials answer the requirements of human tissue and blood compatibility in full measure [1, 2]. The primary efforts in this area are bended to the development of modification methods of membranes using a wide number of physical, chemical and physicochemical methods as well as nanostructuring. It is known that in contact of a foreign material with blood there is formed a blood plasma layer on its surface; the dynamics of composition and structure variation of this layer defines in many respects the physicochemical and biocompatible properties of membrane. It is supposed that at contact with blood the hemocompatible materials should have a minimum value of free interface energy and identical modes of distribution of polar and dispersive components of free surface energy of material and blood (plasma protein) accordingly ("complementarity hypothesis") [2]. On the fulfillment of these conditions the surface adsorbs a minimum of protein which is metabolizable with plasma protein; that leads finally to the increase of material hemocompatibility. The biological structures, especially cell membranes, include hydrophile and hydrophobic domains of size from 10 - 50 nanometers to the angstrom units of mosaic kind. It is supposed, that the simulation of structures of this kind on the polymer membrane surfaces will allow running up to the necessary energy and structural parameters of the surface as well as to the bio- and hemocompatibility of products with a high probability [3]. In this work is investigated the influence of three perspective methods of surface modification of polymers on the bio-and hemocompatibility. The samples for the hemocompatibility investigation were selected according to the hemolysis number (the influence of polymer surface on the erythrocyte lysis/destruction) induced by the polymer surface. For the quantitative criterion was taken the hemolysis relative number a_r in percentage terms. The adhesion and activation registration of thrombocytes was realized after the samples incubation in the citrated (9:1) human blood plasma enriched by thrombocytes, and after their photographing on an electronic scanning microscope Jeol-300 (Japan). For the quantitative characteristic was taken the relative number of thrombocyte adhesion. The thrombocyte activation degree on the investigated membrane surface was defined as a relation of cell quantity in the strongly activated form (completely spread-eagle cells and aggregates) to the total adherent thrombocytes expressed in percentage terms.

There were realized comparative investigations of the influence of surface modification of membranes on the basis of polyethylene and polyamide by the methods of plasmachemical treatment and chemical modification by fluorination and sulfonation in various technological options on the interaction with blood components [4, 5]. For the variation of the influence depth of these methods on the membrane surface were chosen the various processing times at the optimum values of the other parameters of modification processes. There were defined the observable changes of some surface characteristics of polyethylene, such as the limiting wetting angle on water, the surface energy and the surface layer morphology. It was shown that these changes are symbatic by nature. It was studied the influence of the methods of polyethylene processing on the hemocompatibility parameters of the modified surface, such as the degree of hemolysis, induced by contact with a foreign surface, the number of the adherent thrombocytes and their activation degree. All three studied methods of modification have shown the possibility of a considerable improvement of hemocompatibility parameters; but the most perspective is the method of surface fluorination, providing the maximum increase of

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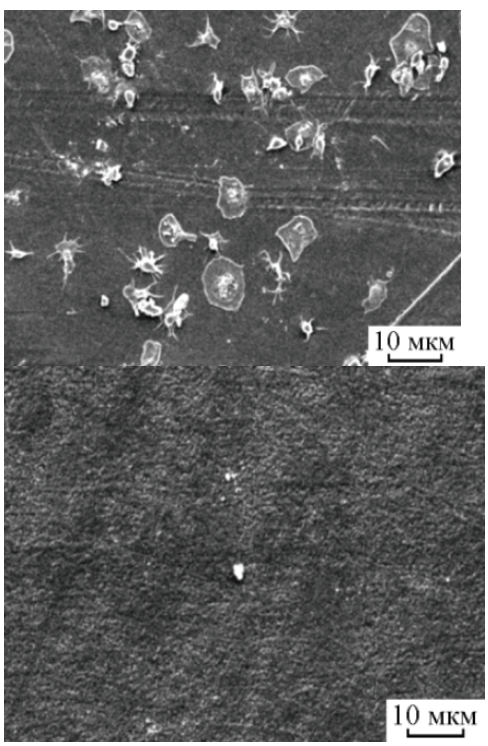
hemocompatible properties and allowing modifying the finished products of various forms and sizes.

On the figure 1 are shown the photos illustrating the changes of adhesion and activation nature of thrombocytes on membranes surface as a result of their modification. The processing by all offered methods is accompanied by the decrease of the number of adherent thrombocytes; that is evidence of the increase of hemocompatible properties on the modified surface.

As evident from the table 1, all investigated samples satisfy the criteria for the selection according to the test of human erythrocyte hemolysis degree, induced by contact with a foreign surface. The number of adherent thrombocytes and the degree of their activation decrease as a result of fluorination of polyethylene surface. But the dependence of the degree of manifestation of these changes on the time of fluorination is extreme by nature, e.g. the minimum adhesion and activation degree of the adherent thrombocytes is observed at the time of processing of 60 minutes. In comparison with the processing in glow-discharge plasma provides the method of surface fluorination more explicit decrease of both the total adherent thrombocytes (criterion of the relative number of thrombocyte adhesion) and the degree of their activation. The sulfonation tells ambiguously on the parameters of interaction of polyethylene surface with thrombocytes (tab. 1). So the number of the adherent cells at the processing time of 30 minutes is a minimum, whereas the degree of their activation is a maximum.



a b

Fig. 1. Photomicrography of the original (a) and fluorinated (b, number 6 in the table 1) membrane samples after contact with blood plasma

All three methods of modification of membranes have shown a possibility of a significant improvement of surface hemocompatibility values; that is connected with the changes of the surface energy, the surface morphology and the formation of mosaic hydrophilic and

hydrophobic structures. At the same time depends the character of the hemocompatibility change of polymer on the processing conditions and is different for each of the used methods. As the most perspective should be recognized the fluorination method; the application of this method, including in mix with other gases, for processing of membranes allows to achieve the maximum effect in the view of the increasing of hemocompatible properties of membranes.

Table 1. The parameters of hemocompatibility of the original and the modified membranes on the basis of polyethylene

No.	Processing	Processing time, minutes	Relative number of thrombocyte adhesion	Activation degree, %	a_r, %
1	Unprocessed	-	1.0 ± 0.1	73	< 0,01
2	Glow-discharge plasma	1	0.09 ± 0.02	65	< 0,01
3	Glow-discharge plasma	3	0.05 ± 0.01	36	< 0.01
4	Glow-discharge plasma	5	0.17 ± 0.04	64	0.41
5	Fluorination	5	0.38 ± 0.09	43	< 0.01
6	Fluorination	15	0.17 ± 0.04	46	< 0.01
7	Fluorination	60	0.02 ± 0.01	7	< 0.01
8	Fluorination	180	0.09 ± 0.03	49	0.01
9	Sulfonation	5	0.62 ± 0.18	32	< 0.01
10	Sulfonation	30	0.03 ± 0.01	69	< 0.01
11	Sulfonation	120	0.28 ± 0.04	47	< 0.01

The primary requirement, made to the new microfiltration membranes for the production of medicaments, is the ability of the latter for the repeated thermal sterilization. The modified membranes MMK-0,2 withstand more than ten sterilization cycles by the saturated steam in an autoclave at the temperature of 120 ºC without change of mechanical and structurally filtration characteristics.

Consequently the original filtration elements, produced by the "Technofiltr" company, have a sterilization ability in relation to the test microorganism Brevundimonas Diminuta, strain PCI 818 (Pseudomonas Diminuta ATCC 19146, DSM 1635) even after 10 autoclaving cycles in pharmacopoeia regime.

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